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Date: May 21, 2010

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Before the Board of Patent Appeals and Interferences

Appellant: David C. Schwartz, *et al.*	April 29, 2010
Serial No.: 10/713,898	Art Unit: 1637
Filing Date: October 18, 2002	Examiner: Stephanie K. Mummert
Title: MICRO FLUIDIC SYSTEM FOR SINGLE MOLECULE IMAGING	File No.: 960296.99047
Confirmation No.: 4216	

APPELLANT'S BRIEF ON APPEAL

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
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Sir:

In response to a final Office Action mailed December 2, 2009 rejecting Appellant's claims for a second time, Appellant David C. Schwartz *et al.*, having filed a timely Notice of Appeal on March 2, 2010 in the above-identified patent application, submits this Brief on Appeal.

I. REAL PARTY IN INTEREST

The real party in interest is assignee Wisconsin Alumni Research Foundation, a non-stock, non-profit Wisconsin corporation located at 614 Walnut Street, Madison, WI 53707-7365, as evidenced by the assignment recorded at Reel/Frame No. 014426/0039.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

III. STATUS OF CLAIMS

Claims 22 and 25 have been cancelled; Claims 1-20 and 28-33 have been withdrawn from consideration; Claims 21, 23, 24, 26 and 27 are pending and under consideration. This appeal is taken with respect to Claims 21, 23, 24, 26 and 27, set forth in Appendix A hereto.

IV. STATUS OF AMENDMENTS

All amendments have been entered.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

A. RELATION OF INDEPENDENT CLAIM 21 TO THE DESCRIPTION.

The claimed subject matter relates to methods for manipulating molecules and, in particular, to a fluid transport system useful for straightening, aligning, and fixing long chain polymers (page 2, lines 10-12; page 3, lines 25-26).

Claim 21 is directed at a method of straightening and fixing polymeric molecules having first and second ends (page 4, lines 4-5 and lines 11-12; page 9, line 2). The method comprises the steps of:

(a) putting the polymeric molecules in a carrier liquid (page 6, lines 3-4; FIG. 1; FIG. 11);

(b) passing the polymeric molecules and carrier liquid through a micro-channel having a first wall electrostatically attractive to the polymeric molecule to promote a laminar flow of carrier liquid in the micro-channel that straightens the polymeric molecule over its length

until at least the first and second ends of the molecule attach to the first wall (page 4, lines 4-10); and

(c) detaching the first wall from the micro-channel (page 4, line 24).

VI. GROUND OF REJECTION TO BE REVIEWED ON APPEAL

THE PRIOR ART REJECTIONS UNDER 35 U.S.C. 103(a).

A rejection of Claims 21, 23-24 and 27 for alleged obviousness is maintained for the reasons set forth in the final office action dated December 2, 2009 (Office Action dated December 2, 2009, page 5, line 2-page 12, line 4).

A. Claims 21, 23-24 and 27 remain rejected under 35 U.S.C. §103(a) as unpatentable over a combination of Perkins *et al.* (Science, Vol. 268:83-87 (1995)) in view of Bensimon *et al.* (US Patent No. 6,265,153).

B. Claim 26 remain rejected under 35 U.S.C. §103(a) as unpatentable over a combination of Perkins *et al.* in view of Bensimon *et al.* and further in view of Kaiser *et al.* (J. Mol. Biol. 6:141-147 (1963)).

VII. ARGUMENT

A. CLAIMS 21, 23-24 AND 27 ARE NOT OBVIOUS UNDER 35 U.S.C. 103(A) OVER A COMBINATION OF PERKINS WITH BENSIMON.

1. The Examiner's rejection.

In alleging obviousness, the Examiner combined two documents. According to the Examiner, Perkins teaches a method of straightening and fixing polymeric molecules by putting the polymeric molecule in a carrier liquid having first and second ends, and passing the polymeric molecules and carrier liquid though a micro-channel having a first wall to promote a laminar flow of carrier liquid in the micro-channel that straightens the polymeric molecule over the length until at least the first end of the molecule attach (Office Action dated December 2, 2009, page 5, line 14-page 6, line 3). The Examiner admitted that Perkins does not teach that the polymeric molecule adheres electrostatically to the first wall of the channel (Office Action dated

December 2, 2009, page 6, lines 16-17) but states that Bensimon teaches a first wall electrostatically attractive to the polymeric molecule (Office Action dated December 2, 2009, page 6, line 22-page 7, line 1). The Examiner further admits that neither Perkins nor Bensimon teaches "detaching the first wall from the micro-channel" (Office Action dated December 2, 2009, page 8, lines 14-15) but alleged that this step was obvious because Bensimon teaches analyzing straightened molecules on a slide (Office Action dated December 2, 2009, page 8, lines 15-20).

The Examiner alleged that it would have been prima facie obvious to one skilled in the art to combine Perkins and Bensimon and to modify them such as to arrive at Appellant's invention (Office Action dated December 2, 2009, page 8, line 21-page 9, line 2). The Examiner alleged that the claim limitation "detaching the first wall from the micro-channel," not taught by either document, was obvious because it was well known to one of ordinary skill in the art at the time the invention was made to remove a bead or other surface from a support (Office Action dated December 2, 2009, page 9, lines 13-17).

2. Summary of Appellants' arguments.

At issue in this appeal is whether the documents cited by the Examiner teach or suggest Appellant's claim limitations such as "micro-channel," "laminar flow," attaching a molecule by at least its first and second end, and "detaching the first wall from the micro-channel" in context of the claimed method. The two documents cited in combination teach methods of elongating or straightening molecules but do not teach or suggest several claim limitations and, in fact, teach away from combining and modifying the cited documents to arrive at Appellant's invention. The Examiner, thus, failed to meet the standard required to show obviousness, as articulated by this Board in *Ex Parte Whalen II*, Appeal 2007-4423, July 23, 2008.

3. It is not obvious from Perkins and Bensimon to straighten and fix polymeric molecules having first and second ends by putting the polymeric molecules in a carrier liquid, passing the polymeric molecules and carrier liquid through a micro-channel having a first wall electrostatically attractive to the polymeric molecule to promote a laminar flow

of carrier liquid in the micro-channel that straightens the polymeric molecule over its length until at least the first and second ends of the molecule attach to the first wall; and detaching the first wall from the micro-channel, as claimed.

(a) Perkins and Bensimon do not teach or suggest using micro-channels.

The invention is nonobvious over Perkins and Bensimon because neither document, either alone or in combination, teaches or suggests using micro-channels. Appellant's invention employs micro-channels sized to provide laminar flow of a liquid to straighten polymeric molecule and to adhere it to the wall of the micro-channel. According to the Examiner, Perkins teaches passing the polymeric molecule through a micro-channel (Office Action, page 5, line 20). However, Perkins does not teach or suggest micro-channels (Office Action, page 6, line 11). The Examiner failed to identify any structure that allegedly constitutes a micro-channel. Perkins investigates deformation of polymers subjected to hydrodynamic flows (Perkins, Abstract; page 83, left column). Perkins teaches stretching a polymer by attaching it with one end to a stationary latex microsphere and translating fluid past it (Perkins, page 83, right column). However, Perkins does not so much as mention using micro-channels. In fact, using a micro-channel in combination with Perkins' method would be greatly impractical as Perkins teaches keeping the polymer away from any surface, a formidable task when the polymer is inside a micro-channel. Also, the Examiner did not explain how a sphere to which Perkins' polymer is tethered could be used inside a micro-channel.

According to the Examiner, Bensimon teaches attaching the molecule to the first wall of the micro-channel (Office Action, page 6, fourth paragraph). However, Bensimon does not teach or suggest using micro-channels and, as such, cannot teach or suggest attaching the molecule to a first wall of the micro-channel.

(b) Perkins and Bensimon, separately or in combination, do not teach or suggest laminar flow.

The invention is nonobvious over Perkins and Bensimon because neither document, either alone or in combination, teaches or suggests using laminar flow. Appellant's invention employs laminar flow to straighten the polymeric molecule and to adhere it to the micro-channel wall.

According to the Examiner, Perkins teaches elongating DNA molecules in laminar flow (Office Action, page 5, line21; page 6, line 11). However, Perkins does not teach or suggest laminar flow. In fact, Perkins' microspheres create turbulence (Perkins, legend to FIG. 1B; page 84, right column) inconsistent with laminar flow. Bensimon teaches using capillary action/convection, principally caused by evaporation at a trailing edge of a liquid, to create a meniscus that aligns polymeric molecules attached to a surface (Bensimon, FIG. 6; Column 2, lines 59-68; Column 17, lines 41-45; Column 19, lines 30-32). In fact, Bensimon explicitly teaches away from using laminar flow, as explained below. Because neither Perkins nor Bensimon teach or suggest using laminar flow to elongate and fix polymeric molecules within micro-channels, and because Bensimon, in fact, teaches away from using laminar flow, a combination of these two documents cannot render obvious the claimed invention.

(c) Perkins and Bensimon do not teach or suggest laminar flow straightening the polymeric molecule over its length until at least the first and second ends of the molecule attach to the first wall.

Perkins teaches DNA tethered to latex microspheres, not to the wall of a micro-channel. Further, Perkins does not teach attachment of the length of the molecule to the micro-channel wall, as the Examiner alleged. Perkins' legend to Figure 1 and footnote 26 that the Examiner relied upon merely state that the molecule was tethered to a latex sphere at one end and deformed by constant fluid flow. In fact, Perkins teaches attaching a DNA molecule to a microsphere at one end "while the other end remains free" (Perkins, page 83, right column, second paragraph). In contrast, Appellant's claims recite that at least the first and second ends of the molecule attach to the micro-channel wall.

Likewise, Bensimon does not teach or suggest using micro-channels, as the Examiner alleged (Office Action, page 6, fourth paragraph). Bensimon teaches elongating polymeric molecules on coverslips, not the walls of micro-channels. Bensimon cannot teach or suggest attaching the molecule to a first wall of the micro-channel because Bensimon does not teach micro-channels in the first place.

Bensimon also does not teach using laminar flow to attach the molecule. First, as discussed above, Bensimon does not teach laminar flow and, in fact, teaches away from using laminar flow. Second, Bensimon's molecules are attached to a surface before they are contacted by a liquid (Bensimon, FIG. 1, FIG. 3, column 1, lines 51-53;). Thus, according to Bensimon's method, the moving liquid does not cause attachment of the molecule but merely aligns the molecule.

(d) Perkins and Bensimon, separately or in combination, do not teach or suggest detaching the first wall form the micro-channel.

Neither Perkins nor Bensimon teaches or suggests detaching the first wall from the micro-channel, as the Examiner herself acknowledged. As explained above, Perkins does not teach or suggest micro-channels and, as such, cannot suggest removing a micro-channel wall. The Examiner alleged that Bensimon by teaching YACs denatured between two cover slips makes obvious this limitation (Office Action, page 9, lines 18-21). However, Bensimon does not teach micro-channels, much less removing a wall therefrom. The passage of Bensimon relied upon by the Examiner (Office Action, page 8, lines 16-17; page 9, lines 21-22) merely teaches dipping cover slips into a DNA-agarose solution and subsequently removing the cover slips at 170 μm/sec to align the YAC molecules (Bensimon, column 19, lines 21-26). Even if two cover slips were equivalent to a micro-channel, which they are not, Bensimon does not teach removing one from the other because individual cover slips are used. Bensimon merely teaches removing cover slips from a solution. The Examiner failed to explain how removing cover slips from a solution makes obvious to one of skill in the art to remove the wall of a micro-channel.

Further, while Bensimon teaches using two cover slips for the hybridization procedure that the Examiner referenced, the two cover slips are "sealed with rubber cement" such as to prevent separation (Bensimon, column 19, lines 41-49). As such, Bensimon cannot make obvious detaching a wall. Further, to the extent that two cover slips are equivalent to a micro-channel, as the Examiner alleged, Bensimon expressly teaches away from using micro-channels by teaching that "the integrity of the molecules thus aligned [on a single cover slip] is better than by evaporation after deposition between two cover slips" (Bensimon, column 19, lines 26-28).

(e) Perkins and Bensimon teach away from the Examiner's proposed combination and modification of the documents.

Perkins and Bensimon explicitly teach away from the suggested combination and required modifications. Bensimon expressly teaches away from using laminar flow, as recited by Appellant's claims, by teaching that using the flow type used in Appellant's invention is "much less efficient than the use of the meniscus" (Bensimon, Column 4, lines 18-20). Instead, Bensimon directs the reader to choose capillary flow/convection, a technique very different from that claimed by Appellant. Paragraph [0050] of Appellant's specification explains the differences between capillary flow/convection and the laminar flow used in Appellant's invention.

Perkins expressly teaches away from adhering at least two ends of the molecule to a surface. The Examiner admits that neither document teaches or suggests detaching the wall from the micro-channel to which the molecule is attached by at least two of its ends, but alleged that it was obvious to do so because Bensimon allegedly teaches analysis of a molecule stretched out on a surface. However, Perkins explicitly teaches away from adhering at least the first and second ends of the molecule to a surface by stating that the molecule "was positioned away from any surface" (Perkins, page 83, second column, second paragraph, emphasis added). Also, Perkins expressly notes that the molecule is attached by only one end "while the other end remains free" (Perkins, page 83, right column, second paragraph).

Bensimon also explicitly teaches away from Perkins' method because Perkin's "method is expensive, is limited to only one molecule at a time, and is difficult to carry out by non-qualified staff" (Bensimon, column 1, lines 25-39). As such, Bensimon teaches away from a combination with Perkins.

B. CLAIM 26 IS NOT OBVIOUS UNDER 35 U.S.C. 103(A) OVER A COMBINATION OF PERKINS WITH BENSIMON AND KAISER.

1. The Examiner's rejection.

In alleging obviousness of Claim 26, the Examiner applied Perkins and Bensimon as outlined in Section A.1. above. The Examiner relied on Kaiser for allegedly teaching treating the

polymeric molecule with a condensation agent to collapse the polymeric molecules into shear resistant balls and wherein step (a) includes the step of placing the polymeric molecules and carrier liquid into a reservoir attached to the micro-channel and decondensing the polymeric molecules in the reservoir prior to step (b). According to the Examiner, it was obvious to one of skill in the art to combine Kaiser with Perkins and Bensimon because Kaiser teaches that spermine protects DNA from breakage caused by rapid stirring (Office Action, page 11, lines 8-13) and because Perkins teaches that visualizing the polymer's chain conformation is useful for studying deformation and that the imaging system has linear gain, allegedly demonstrating that Perkins was motivated to maintain the polymer sequence in an intact linear format to measure length and flow rate (Office Action, page 11, lines 13-20).

2. Summary of Appellants' arguments.

A combination of Perkins and Bensimon does not teach Appellant's invention, as outlined above. Regardless of whether Kaiser teaches the additional limitations recited in Claim 26, Kaiser does not make up for the shortcomings of Perkins and Bensimon as it contemplates neither laminar flow nor micro-channels. Further, Kaiser fails to teach decondensing the molecule in a reservoir attached to the micro-channel, as recited by Claim 26.

3. It is not obvious from Perkins, Bensimon, and Kaiser to straighten and fix polymeric molecules having first and second ends by putting the polymeric molecules in a carrier liquid, treating the polymeric molecules with a condensation agent, decondensing the molecule in a reservoir attached to a micro-channel, passing the polymeric molecules and carrier liquid through the micro-channel having a first wall electrostatically attractive to the polymeric molecule to promote a laminar flow of carrier liquid in the micro-channel that straightens the polymeric molecule over its length until at least the first and second ends of the molecule attach to the first wall; and detaching the first wall from the micro-channel, as claimed.

Claim 26 is rejected for alleged obviousness over Perkins, in view of Bensimon, and in further view of Kaiser. A combination of Perkins and Bensimon does not teach Appellant's

invention, as outlined above. Kaiser teaches treating polymeric molecules with a condensation agent but fails to teach the remaining limitations of Claim 26, not addressed by the Examiner. Kaiser contemplates neither laminar flow nor micro-channels. Kaiser also does not teach placing the polymeric molecules and carrier liquid into a reservoir attached to the micro-channel. Kaiser also fails to teach decondensing the polymeric molecules in the reservoir prior to step (b). The Examiner failed to demonstrate how the cited documents teach or suggest these limitations.

For these reasons, Appellant's methods of straightening and fixing polymeric molecules using laminar flow of carrier liquid in a micro-channel that straightens the polymeric molecule until at least the first and second ends of the molecule attach to the micro-channel wall, including decondensing the molecule in a reservoir attached to the micro-channel is nonobvious over Perkins, Bensimon, and Kaiser because none of these documents, either alone or in combination, teaches or suggests the recited claim limitations.

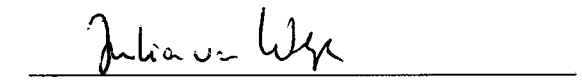
F. SUMMARY

Appellants here demonstrate that the documents cited by the Examiner fail to disclose the elements of Appellants' methods, lack any suggestion to modify their teachings to meet the claims, and, in fact, teach away from Appellant's invention. Neither Perkins, Bensimon, or Kaiser, alone or in combination, discloses, teaches, or suggests using laminar flow of carrier liquid in a micro-channel to straighten a polymeric molecule over its length until at least the first and second ends of the molecule attach to the first wall and detaching the first wall from the micro-channel. Further, neither Perkins, Bensimon, or Kaiser, alone or in combination, discloses, teaches, or suggests decondensing the molecule in a reservoir attached to the micro-channel.

Perkins and Bensimon expressly teach away from Appellant's invention. Bensimon expressly teaches away from using laminar flow as "much less efficient" than Bensimon's method and Perkins expressly teaches away from adhering at least two ends of the molecule to a surface. For these reasons, the claimed methods are not rendered obvious by the cited documents and the rejections should be withdrawn.

In view of the above, Appellants respectfully ask the Board to reconsider and reverse the Examiner's rejections.

Respectfully submitted,

By: 

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APPENDIX A
Claims on Appeal in Patent Application No. 10/713,898

21. (Previously presented) A method of straightening and fixing polymeric molecules having first and second ends, the method comprising the steps of:

(a) putting the polymeric molecules in a carrier liquid;

(b) passing the polymeric molecules and carrier liquid through a micro-channel having a first wall electrostatically attractive to the polymeric molecule to promote a laminar flow of carrier liquid in the micro-channel that straightens the polymeric molecule over its length until at least the first and second ends of the molecule attach to the first wall; and

(c) detaching the first wall from the micro-channel.

23. (Previously presented) The method of claim 21 further including the step of (d) applying restricting enzymes to the straightened polymeric molecule attached to the first wall.

24. (Previously presented) The method of claim 21 further including the step of (d) optically inspecting the straightened polymeric molecule attached to the first wall.

26. (Original) The method of claim 21 wherein the polymeric molecules are treated with a condensation agent to collapse the polymeric molecules into shear resistant balls and wherein step (a) includes the step of placing the polymeric molecules and carrier liquid into a reservoir attached to the micro-channel and decondensing the polymeric molecules in the reservoir prior to step (b).

27. (Original) The method of claim 21 further including the step of treating at least one wall of the micro-channel to have a positive surface charge of predetermined density.

APPENDIX B
Factual Evidence in Patent Application No. 10/713,898
Submitted as part of Appeal Brief

APPENDIX C
Related Proceedings in Patent Application No. 10/713,898

Submitted as part of Appeal Brief